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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/456,693	12/09/1999	DASA LIPOVSEK	50036/021002	6778

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EXAMINER

WESSENDORF, TERESA D

ART UNIT

PAPER NUMBER

1639

DATE MAILED: 03/13/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/456,693

Applicant(s)

LIPOVSEK, DASA

Examiner

T. D. Wessendorf

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 09 January 2003.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1 and 8-52 is/are pending in the application.
- 4a) Of the above claim(s) 13-52 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1 and 8-12 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
- If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
- a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) 8, 13.
- 4) ☐ Interview Summary (PTO-413) Paper No(s). _____.
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

The request for a continued prosecution application (CPA) under 37 CFR 1.53(d) filed on [11/19/02] is acknowledged. 37 CFR 1.53(d)(1) was amended to provide that the prior application of a CPA must be: (1) a utility or plant application that was filed under 35 U.S.C. 111(a) before May 29, 2000, (2) a design application, or (3) the national stage of an international application that was filed under 35 U.S.C. 363 before May 29, 2000. *See Changes to Application Examination and Provisional Application Practice*, interim rule, 65 Fed. Reg. 14865, 14872 (Mar. 20, 2000), 1233 Off. Gaz. Pat. Office 47, 52 (Apr. 11, 2000). Since a CPA of this application is not permitted under 37 CFR 1.53(d)(1), the improper request for a CPA is being treated as a request for continued examination of this application under 37 CFR 1.114. *See id.* at 14866, 1233 Off. Gaz. Pat. Office at 48.

Election/Restrictions

Restriction to one of the following inventions is required under 35 U.S.C. 121:

- I. Claims 1 and 8-12 drawn to a library of scaffold-based proteins.
- II. Claims 13-17, drawn to a fused library.

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III. Claims 18-20, drawn to a library covalently bound to nucleic acid.

IV. Claim 21, drawn to a multimer protein in a library.

V. Claim 22, drawn to a library formulated with a physiologically acceptable carrier.

The inventions are distinct, each from the other because of the following reasons:

Inventions I and II-V are unrelated. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different modes of operation, different functions, or different effects (MPEP § 806.04, MPEP § 808.01). In the instant case the different inventions are drawn to structurally different protein libraries. The library of Group I contains a non-fusion protein library. The libraries of Groups II-V contain a fusion or covalently bound or multimer protein library. Thus, the non-fusion of Group I is distinct and different from the structure and/or components present in groups II-V.

Because these inventions are distinct for the reasons given above and have acquired a separate status in the art because of their recognized divergent subject matter, and the search required for Group I is not required for Groups II-V, restriction for examination purposes as indicated is proper.

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This application contains claims directed to the following patentably distinct species of the claimed invention:

If Group II is elected, applicants are to elect the different heterologous compounds fused to the proteins in a library as recited in claims 14-17.

Each of the species fused with the proteins in the library differs in structure, mode of actions and/or function. A prior art reference anticipating one species would not render obvious the other species.

Applicant is required under 35 U.S.C. 121 to elect a single disclosed species for prosecution on the merits to which the claims shall be restricted if no generic claim is finally held to be allowable. Currently, claims 1 and 13 are generic.

Applicant is advised that a reply to this requirement must include an identification of the species that is elected consonant with this requirement, and a listing of all claims readable thereon, including any claims subsequently added. An argument that a claim is allowable or that all claims are generic is considered nonresponsive unless accompanied by an election.

Upon the allowance of a generic claim, applicant will be entitled to consideration of claims to additional species which are written in dependent form or otherwise include all the

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limitations of an allowed generic claim as provided by 37 CFR 1.141. If claims are added after the election, applicant must indicate which are readable upon the elected species. MPEP § 809.02(a).

Should applicant traverse on the ground that the species are not patentably distinct, applicant should submit evidence or identify such evidence now of record showing the species to be obvious variants or clearly admit on the record that this is the case. In either instance, if the examiner finds one of the inventions unpatentable over the prior art, the evidence or admission may be used in a rejection under 35 U.S.C. 103(a) of the other invention.

During a telephone conversation with K. Elbing on 2/26 and 3/6/03 a provisional election was made with traverse to prosecute the invention of Group I, claims 1 and 8-12. Affirmation of this election must be made by applicant in replying to this Office action. Claims 13-22 are withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to a non-elected invention.

Status of Claims

Claims 1 and 8-52 are pending in the application.

Claims 2-7 have been cancelled in the Amendment of 2/1/02.

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Claims 13-52 are withdrawn from consideration as being drawn to non-elected inventions.

Claims 1 and 8-12 are under examination.

Specification

The specification has not been checked to the extent necessary to determine the presence of all possible minor errors (typographical, grammatical and idiomatic). Applicant's cooperation is requested in correcting any errors of which applicant may become aware in the specification.

Claim Rejections - 35 USC § 101

35 U.S.C. 101 reads as follows:

Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claims 1 and 8-12 are rejected under 35 U.S.C. 101 because the claimed invention is not supported by either a specific asserted utility or a well established utility.

The specification fails to provide a specific utility for the claimed library of scaffold-based proteins. The disclosure provides a generalized statement that the library is useful for screening. However, the exemplification is nil. Notwithstanding this, screening is not a specific utility. Basically all collections of any kind undergo screening. The essential aspect

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of screening is the discovery of a new product known to possess the specific utility. The screening of a library can be likened to screening nature's collection of naturally occurring products, yielding useful product. The court in *Brenner v. Manson*, 148 U.S.P.Q. 689 (1966), expressed the opinion that all chemical compounds are "useful" to the chemical arts when this term is given its broadest interpretation. However, the court held that this broad interpretation was not the intended definition of "useful" as it appears in 35 U.S.C. §101, which requires that an invention must have either an immediately apparent or fully disclosed "real world" utility...A patent is not a hunting license. . . .[i]t is not a reward for the search, but compensation for its successful conclusion. "Congress intended that no patent be granted on a chemical compound whose sole 'utility' consists of its potential role as an object of use-testing." *Brenner*, 148 USPQ at 696. The court held that:

The basic quid pro quo contemplated by the Constitution and the Congress for granting a patent monopoly is the benefit derived by the public from an invention with substantial utility. . . . [u]nless and until a process is refined and developed to this point-where specific benefit exists in currently available form-there is insufficient justification for permitting an applicant to engross what may prove to be a broad field. . . . In *Brenner*, the Court approved a rejection for failure to disclose any utility for a compound where the compound was undergoing screening for possible compounds the utility of which has also not been identified. *Brenner*, 148 USPQ at 690. (Emphasis ours).

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Claims 1 and 8-12 are also rejected under 35 U.S.C. 112, first paragraph. Specifically, since the claimed invention is not supported by either a specific asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention.

Claim Rejections - 35 USC § 112, first paragraph

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1 and 8-12 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The specification fails to provide an adequate written description for a library wherein the proteins comprised basic-neutral-acidic motif that replaces an integrin-binding motif. It is not apparent from the description in the specification as to

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the criteria by an amino acid is defined as basic, neutral or acidic. Because the single disclosed motif, Ser-Gly-glutamate would appear not to be within the scope of the disclosed genus. Ser is not an art-recognized basic residue. Neither is glutamate known to be an acidic residue. Also, the specification fails to provide a description for a library of scaffold-based proteins. The specification, page 13, line 6 recites for a fibronectin-based scaffold. These are two different concepts.

Claim Rejections - 35 USC § 112, second paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1 and 8-12 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

A. In claim 1, the phrase "scaffold-based proteins" is unclear. It is not clear as to what constitutes a scaffold-based protein, especially in the absence of positive support in the specification. Cf. with page 13, line 6 of the specification which recites a fibronectin-based scaffold.

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B. The metes and bounds of the claimed basic-neutral-acidic residues, in the context of the claimed, are unclear. Claim 10.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless -

(e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 1 and 8-12 are rejected under 35 U.S.C. 102(e) as being anticipated by Koide [2002/0019517 which is the same as (U.S. 6,462,189)].

Koide discloses at paragraphs [0022]-[0028] a fibronectin type m (Fn3) polypeptide monobody comprising a plurality of Fn3 .beta.-strand domain sequences that are linked to a plurality of loop region sequences. One or more of the monobody loop region sequences of the Fn3 polypeptide vary by deletion, insertion or replacement of at least two amino acids from the corresponding loop region sequences in wild-type Fn3. The .beta.-strand domains of the monobody have at least about 50% total amino acid

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sequence homology to the corresponding amino acid sequence of wild-type Fn3's .beta.-strand domain sequences. One or more of the loop regions of the monobody comprise amino acid residues: i) from 15 to 16 inclusive in an AB loop; ii) from 22 to 30 inclusive in a BC loop; iii) from 39 to 45 inclusive in a CD loop; iv) from 51 to 55 inclusive in a DE loop; v) from 60 to 66 inclusive in an EF loop; and vi) from 76 to 87 inclusive in an FG loop(at least three randomized loops, as claimed). Koide discloses at paragraph [0089] the used of Fibronectin type III domain (Fn3) as scaffold (as in claim 1). Koide describes at paragraph [0091] Fn3 does not have disulfide bonds (as in claim 12). Koide discloses that 17 Fn3 domains are present just in human fibronectin that provides important information on conserved residues which are often important for the stability and folding. Large variations are seen in the BC and FG loops. Koide further discloses that NMR studies have revealed that the FG loop is highly flexible. The flexibility has been implicated for the specific binding of the 10th Fn3 to afa integrin through the Arg-Gly-Asp (RGD) motif. Koide describes at paragraph [0092] that the tenth type III module of fibronectin has a fold similar to that of immunoglobulin domains. Koide, paragraph [0129], describes that the amino acid sequence of defined regions of Fn3 were randomized to construct

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a library. See further the Examples, specifically the Tables. The tables show the different amino acid substitutions for the integrin binding motif, RGD. See also the claims, particularly, claims 15-29. Accordingly, the specific fibronectin-based scaffold of Koide with random amino acid loops at the tenth module of Fn3 fully meets the broad claimed scaffold-based proteins.

No claims are allowed.

REASSIGNMENT OF LOCATION

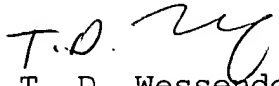
The Art Unit location of your application in the USPTO has changed. To aid in correlating any papers for this application, all further correspondence regarding this application should be directed to Art Unit **1639**.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to T. D. Wessendorf whose telephone number is (703) 308-3967. The examiner can normally be reached on Flexitime.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Andrew Wang can be reached on (703) 306-3217. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 308-7924 for regular communications and (703) 308-7924 for After Final communications.

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Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.


T. D. Wessendorf
Primary Examiner
Art Unit 1639

tdw
March 7, 2003